UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/942,117	08/30/2001	Andreas Menrad	SCH-1832	6934

23599 7590 06/02/2003

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	18

DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/942,117	MENRAD ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above claim(s) *17-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 5/16/03 (Paper No. 16), is acknowledged.

2. Claims 1-55 are pending.

3. Claims 17-55 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

4. Claims 1-16 are under examination as they read on a protien that has the ability to bind specifically to the ED_b-fibronectin domains and that has an apparent molecular weight of 120-130 kDa for the light chain and 150-160 kDa for the heavy chain, wherein the binding region comprises the $\alpha 2\beta 1$ chain of the integrin wherein the ED_b-fibronectin binding region is SEQ ID NO: 1 as the species.

5. Applicant's IDS, filed 1/7/03 (Paper No. 14), is acknowledged, however, references B1, and C1-C6 were crossed out as the entire documents were not found. Applicant is invited to produce such documents.

6. The following new ground of rejection is necessitated by the amendment filed on 5/16/03/17/02, paper No. 16.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 6-7, 9-10, 12-13 and 15-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrase "whereby a binding region of said protein comprises the sequence of SEQ ID NO:1" claimed in claims 6, 9, 12 and 15 represent a departure from the specification and the claims as originally filed.

Applicant's amendment filed 5-16-03 does not point to the specification for support for the newly added limitations "whereby a binding region of said protein comprises the sequence of SEQ ID NO:1" as claimed in claims 6, 9, 12, and 15. However, the specification does not provide a clear support of "whereby a binding region of said protein comprises the sequence of SEQ ID NO:1". The specification on page 28, lines 8-11, discloses that SEQ ID NO: 1 peptide is ED-B peptide derived from the ED_b-bibronectin domains, rather than from the protein that

binds to EDb-fibronectin domain as claimed. The instant claims now recite a limitation which was not clearly disclosed in the specification and claims as originally filed.

9. In view of the amendment filed on 5/16/03 (Paper No. 16), only the following rejections remained.

10. 35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 5-16 stand rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter essentially for the same reasons set forth in the previous Office Action, paper No. 13, mailed 1/14/03.

Applicant's arguments, filed 5/16/03 (Paper No. 16), have been fully considered, but have not been found convincing.

Applicant argues that the amendments to the claims rendered the rejection moot. However, claims 5-16 still cite a protein with absence of the hand of man.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the $\alpha 2\beta 1$ protein that has the ability to bind specifically to the ED_b-fibronectin domains for screening assay does not reasonably provide **enablement** for any protein wherein binding to the ED_b-fibronectin domains is inhibited by any "polypeptide" that **comprises** an amino acid sequence of SEQ ID NO:1, and that **comprises** the α chain of the integrin further as recited in claims 1(a-f), 2(a-f), 3(a-f) and 4-16. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim essentially for the same reasons set forth in the previous Office Action, paper No. 13, mailed 1/14/03.

Applicant's arguments, filed 5/16/03 (Paper No. 16), have been fully considered, but have not been found convincing.

Applicant argues that the specification provides guidance to enable one skilled in the art to practice the scope of the claimed invention. Applicant argues that the he is not claiming just any

protein that binds to the EDb-fibronectin domain and said binding is inhibited by a polypeptide that comprises SEQ ID NO:1, has the ability to bind specifically to an EDb-fibronectin domain, that is expressed or activated specifically in endothelial cells, that is expressed or activated specifically in a stormal cell of a tumor, that is expressed or activated specifically in a tumor and that has a specific molecular weight. Further, Applicant argues that the skilled artisan is directed to a specific location where the protein is expressed and the protein has the function of binding to an EDb-fibronectin domain and has a specific MW. Applicant argues that there is not an infinite number of peptides to test and thus there is no undue experimentation. Applicant further argues that the amount of experimentation, if any, is minimal or routine, an dthe specification clearly characterizes the claimed protein.

Applicant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. The claims as written encompass a broad genus of proteins. Further, the enablement issues of making any polypeptide or the EDb-fibronectin domain comprises SEQ ID NO:1 still remain because the specification does not teach and provide sufficient guidance as to which amino acid of SEQ ID NO:1 would have been altered such that the resultant polypeptide would have retained the function of binding to the claimed protein. Therefore, absent the ability to predict which of these protein would function as claimed, and given the lack of data on regions critical for the claimed protein activity, for one of skill in the art to practice the invention as claimed would require a level of experimentation that is excessive and undue.

It is recognized in the prior art that the function of a protein depends on the sequence of its amino acids in a certain pattern, conformation of the protein due to the amino acid sequence and the functional properties of the different parts of the protein. The specification does not teach which protein other than $\alpha 2\beta 1$ would have all the activities of the recited activities. Therefore, the specification fails to provide sufficient guidance as to which other proteins would bind to EDb-fibronectin domain and still maintained the same function as $\alpha 2\beta 1$.

Consequently, without additional guidance in the specification, and the dearth of information in the art, for one of skill in the art to practice the invention as claimed, would require experimentation that is excessive and undue. The amount of guidance or direction needed to enable an invention is inversely related to the mount of knowledge in the state of the art as well as the predictability in the art (In re Fisher, 427 F.2d 833, 839, 166 USPQ 18,24 (CCPA 1970)).

11. Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention essentially for the same reasons set forth in the previous Office Action, paper No. 13, mailed 1/14/03.

Applicant's arguments, filed 5/16/03 (Paper No. 16), have been fully considered, but have not been found convincing.

Applicant argues that an adequate written description is achieved by disclosing relevant identifying characteristics that is structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure or by a combination of such identifying characteristics.

however, there is no described or art-recognized correlation or relationship between the structure of the invention, a protein and it's binding to EDb-fibronectin domains, the feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of proteins that have the ability to bind specifically to an EDb-fibronectin domain, expressed or activated specifically in an endothelial cell, a stormal cell or a tumor or a tumor cell, inhibited by any polypeptide, and has MW of 120-130kDa for ligh chain and 15-160 kDa for the heavy chain determined by SDS gel.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-16 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,583,203, as is evidenced by U.S Patent No. 5,120,830 essentially for the same reasons set forth in the previous Office Action, paper No. 13, mailed 1/14/03.

Applicant's arguments, filed 5/16/03 (Paper No. 16), have been fully considered, but have not been found convincing.

14. Claims 1-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Takada et al (J Cell Biology 105:397-407, 1989), as is evidenced by U.S Patent No. 5,120,830 essentially for the same reasons set forth in the previous Office Action, paper No. 13, mailed 1/14/03.

Applicant's arguments, filed 5/16/03 (Paper No. 16), have been fully considered, but have not been found convincing.

15. Claims 1-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Kern et al (Eur. J. Biochem. 215:151-159, 1993), as is evidenced by U.S Patent No. 5,120,830 essentially for the same reasons set forth in the previous Office Action, paper No. 13, mailed 1/14/03.

Applicant's arguments, filed 5/16/03 (Paper No. 16), have been fully considered, but have not been found convincing.

Applicant argues that the cited references do not form a basis for inherent anticipation. Applicant asserts that inherency cannot be established by probabilities or possibilities. Applicant argues that it must established that the protein of the cited references, which was obtained from placenta or platelets, is the same as the claimed protein, which is specifically expressed or activated in, for example, endothelial cells. Applicant further argues that there is no suggestion or teaching in the cited reference that the two proteins have the same functions or properties.

Applicant has not distinguish the prior art protein from the claimed protein and since the office does not have a laboratory to test the reference $\alpha 2\beta 1$ receptor, it is applicant's burden to show that the reference $\alpha 2\beta 1$ receptor do not bind to ED_b-fibronectin domains as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980). In addition, applicant is invited to consider the following decisions based upon generating antibodies. Whether the rejection is based on "inherence" under 35 U.S.C. § 102 or prima facie obviousness under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. Examiner properly shifted burden to applicant to establish, through objective evidence, that protein of invention differ in unobvious manner from those of the prior art references. Ex parte Phillips, 28 USPQ2d 1302 (BPAI 1993). Here, applicant has not provided any objective evidence to support the difference between the prior art and instant protein. The record does not contain sufficient objective evidence that the referenced $\alpha 2\beta 1$ differ in any significant manner from that claimed.

In response to applicant's argument that "there is no suggestion or teaching in the cited reference that the two proteins have the same functions or properties." If the prior art structure is capable of performing the intended functions or properties, then it meets the claim. For example in Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999); the following was noted. "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art". See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

16. No claim allowed

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
May 29, 2003

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600